REMARKS

Reconsideration of the rejections set forth in the Office Action dated August 10, 2001 is respectfully requested. The applicants petition the Commissioner for a 2-month extension of time: a separate petition accompanies this amendment. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page(s) is/are captioned "Version with markings to show changes made."

I. Amendments

Claim 23 was amended to include the limitation that the antisense compound is administered to the patient by placing the compound in contact with, or injecting the compound into, the treated region of the vessel. The placement of the antisense compound via direct local administration, for the treatment of restensosis, is described generally on page 11, lines 3-21. and with respect to several specific method of localized delivery, on page 11, line 23 to page 14, line 24. As described on page 14, line 33-37, the presently claimed assay method is intended to confirm the presence of antisense compound in target vessel cells "following antisense administration at the vessel site." It is understood by this description of the assay method that antisense administration is via the same routes used for antisense treatment.

Newly added claims 26 and 27 further limit the methods of compound administration to those specifically disclosed on page 11, line 23 to page 14, line 24 (claim 26) and to the method of stent delivery described on page 13, lines 8-23 (claim 27).

No new matter has been added by the claim amendments.

II. Rejections under 35 U.S.C. §112, second paragraph

Claims 23-25 in the application were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The specific rejection applied to claim 23 is respectfully traversed in view of the foregoing amendment and/or following remarks.

Claim 23, and claims 24 and 25 dependent thereon, were rejected as being incomplete for omitting an essential step by which one could determine that the presence of a detected heteroduplex indicates the ability of an antisense compound to reach and interact with *c-myc* in vessel cells. The examiner asserts that it is unclear how the detection of the presence of heteroduplexes in the body fluid of an individual would provide any evidence that the morpholino antisense compound of the instant invention actually reached its *c-myc* target mRNA, specifically in the vessel cells.

Claim 23, as now amended, includes the limitation that the patient is administered the antisense compound by placing the compound in contact with, or injecting the compound into, the treated region of the vessel, thus assuring that the compound is delivered directly to the cells in the treated vessel region with little or no dilution. Accordingly, the method as now amended provides reasonable assurance that at least a portion of the heteroduplex detected in a body fluid reflects uptake of the antisense compound into cells in the target region. For example, if one detected 10% of the administered antisense in heteroduplex form, as suggested on page 11, lines 11-13, and the other 90% in free form, one could be reasonably certain that a large if not predominant portion of the heteroduplex resulted from vessel-cell uptake, since most of the antisense that escaped from the target site without vessel-cell uptake would be cleared in free form.

In view of the claim amendments and foregoing remarks with respect thereto, the applicants submit that the claims now pending in the application meet the requirements of 35 U.S. C. §112, second paragraph. Accordingly, it is requested that the rejections be withdrawn.

In view of the foregoing, the applicant submits that the claims pending in the application are now in condition for allowance. A Notice of Allowance is therefore respectfully requested.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4404.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

23. (Twice Amended) In a method aimed at reducing the risk of restenosis in a region of a patient's coronary vessel which has been treated by coronary angioplasty using a catheter with a distal-end expandable balloon, by administering to the vessel region, an antisense compound directed against a target human *c-myc* mRNA sequence, a method for assaying the ability of the antisense compound to reach and interact with *c-myc* mRNA in patient vessel cells, comprising

administering [to the patient,] a morpholino antisense compound having a substantially uncharged backbone, and a sequence that spans the start codon of the human *c-myc* gene, to the patient, by placing the compound in contact with, or injecting the compound into, the treated region of the vessel,

at a selected time after said administering, taking a sample of a body fluid from the subject,

detecting in said sample the presence of a nuclease-resistant heteroduplex composed of the antisense compound and the target RNA region, and

correlating the presence of detected heteroduplex in said sample with the ability of said antisense compound to reach and interact with *c-myc* mRNA in vessel cells.

-- 26. (New) The method of claim 23, wherein said administering is selected from a group consisting of: (i) contacting the treated region of said vessel with a reservoir containing said antisense compound and introducing said antisense compound from said reservoir into said vessel by iontophoresis, (ii) injecting said antisense compound directly into the vessel by means of an injection balloon catheter, (iii) contacting the treated region of the vessel with an angioplasty catheter balloon having a surface coating of the antisense compound in diffusable form, (iv) contacting the treated region of the vessel with an intravascular stent having a surface coating of the antisense compound in diffusable form, and, (v) delivering directly into vessel tissue microparticles having said antisense compound in releasable form entrapped therein.

27. (New) The method of claim 23 wherein said administering includes contacting the treated region of the vessel with an intravascular stent having a surface coating of the antisense compound in diffusable form.